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FORM PTO-1390 (REV. 11-2000) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	U.S. APPLICATION NO. (If known, see 37 CFR 1.5
LEXSA.P002	09/914257

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/CU00/00001	February 22,2000	February 22, 1999

TITLE OF INVENTION
Composition for theTreatment of Psoriasis

APPLICANT(S) FOR DO/EO/US
Carlos Manuel MIYARES CAO

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [X] The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [X] is attached hereto (required only if not communicated by the International Bureau).
   b. [ ] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [X] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [X] is attached hereto.
   b. [ ] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [ ] Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (to follow)
10. [ ] An English lanugage translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. [X] An Information Disclosure Statement under 37 CFR 1.97 and 1.98. (to follow)
12. [X] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 ~~is included~~. (to follow)
13. [ ] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment.
15. [ ] A substitute specification.
16. [ ] A change of power of attorney and/or address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. [ ] A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [X] Other items or information: (1) sheet of Drawings enclosed
Translator's Declaration (to follow); Small Entity Dec (to follow)
copy of In'tl ap. WO 00/50057A2; Internl Search Report WO 00/50057A3
copy PCT/IPEA/416 containing amendment in the claims
copy of PCT/RO/101 form

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/914257	PCT/CUoo/00001	LEXSA.p0024

21. ☒ The following fees are submitted:	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1000.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$860.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$710.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$690.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 860	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$ 130	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	4 -20 =	-0-	x **$18.00**	$ -0-	
Independent claims	-0- 3 =	-0-	x **$80.00**	$ -0-	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$270.00**	$ -0-	
TOTAL OF ABOVE CALCULATIONS =				$ 990	
☒ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. +				$ 495	
SUBTOTAL =				$ 495	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				$ -0-	
TOTAL NATIONAL FEE =				$ -0-	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$ -0-	
TOTAL FEES ENCLOSED =				$495	
				Amount to be refunded:	$
				charged:	$

a. ☒ A check in the amount of $ 495.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 10-0100. A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Marvin Feldman
Lackenbach Siegel
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SIGNATURE

Marvin Feldman
NAME

25,797
REGISTRATION NUMBER

Certificate of Express Mailing
I hereby certify that this correspondence is being deposited with the United States Postal Service as
EXPRESS MAIL No. EL 135 664 105US
under 37 CFR 1.10 Cerft. in an envelope addressed to:
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Marvin Feldman
Dated: August 22, 2001

Applicant hereby petitions that any and all extensions of the term necessary to render this response timely be granted. Costs for such extension(s) and or any other fee due with this paper, not fully covered by an enclosed check may be charged to Deposit Account #10-0100.

EXPRESS MAILING CERTIFICATE

In re the application of:

APPLICANT:	Carlos Manuel MIYARES CAO
INTERNATIONAL APPLICATION NO:	PCT/CU00/00001
BASED ON PRIORITY APPLICATION NO:	CU 16/99
TITLE:	Composition for the Treatment of Psoriasis
EXPRESS MAIL FILED:	August 22, 2001

#3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

INVENTOR(S): Carlos Cao

TITLE: Composition for the Treatment of Psoriasis

DOCKET NO: P-24 LEXSA

Assistant Commissioner of Patents
Washington, D.C. 20231

TRANSLATOR'S DECLARATION

Sir:

The undersigned, Marietta Crespo, hereby declares: That I am a resident of Havana, Cuba residing at Calle 30 #2306 e/ 25 y 25, Playa, Havana Cuba, Zip Code 11300

That I am conversant in the Spanish and English languages and qualified to prepare an English translation from the corresponding Spanish language document.

That I have translated the attached English document from Spanish and that it is complete and adequate and it is a true and faithful translation of the original Spanish text, and

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and believe are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United State Code, and that such willful false statements may jeopardize the validity of the patent application.

Dated: Sept 18th, 2001

Marietta Crespo
Translator's Signature

CENTRO DE INFORMACION DE LA ENERGIA NUCLEAR C.I.E.N. DIRECCION

1/prts

COMPOSITION FOR THE TREATMENT OF PSORIASIS.

Technical sector

The present invention is related with the branch of the Human Medicine, and with the Dermatology, and in particular with a composition obtained starting from the human placenta with activity in the regulation of the speed of regeneration of the skin, and therefore useful in the treatment of the psoriasis, as well as with the procedure for obtaining said composition.

Prior Art

The psoriasis is not a recently discovered illness. It was classified as the leprosy of the Greeks and as it seems, it existed in Mexico before the conquest (Daune, M.; FSCHS, P.P. La Recherche (1980), 11: 116-1066; International Journal of Dermatology. Vol. 36, No. 4, April 1977). This illness affects all the races and in all the latitudes and it can be presented in a family in the course of several generations (Int. Journal of Dermatology. Vol. 36, No.4, April 1977; Lerner, A. B., et al. Invest. Dermatol. 1975. 20 (2): 299-314, 1953).

The beginning of the illness often it is associated with superficial damages of the skin as burns and scratches. Other factors like low humidity, infections, stress or drugs can precipitate or to exacerbate the psoriasis.

The physical trauma maybe incites an angiogenic factor of change in the vascular fact and the epidermatopoyesis and the neutrophile chimiotasis, and the called tissular psoriatic reaction (Moroni, P., et al. Derm. Beruf. Umwelt, 36 (5) pág. 163-164, 1988).

The climatic factors such as cold have been reported as adverse effects to the psoriasis. In some studies carried out it was bigger the frequency psoriasis in Africa where the climate is dry and the humidity is low (Faber, E. N., et al. Natural Epidemiology. History and genetic psoriasis. Second Ed. Page 231. Edit. Marcel Depper, New York, 1991).

It is very well known that the stress can break out or to exacerbate the psoriasis, although the exact mechanism for that is unknown, however studies based on psiconeuroimmunology can explain it (Moroni, P., et al. Derm. Beruf. Umwelt, 36 (5) Pag. 163-164, 1988).

As a result of the specialized treatment, the lesions can disappear but the relapses are almost sure and tendencies exist to that its effectiveness gradually is lost in each treatment (Lerner, A. B., et al. Invest. Dermatol. 1953, 20 (2): 299-314, 1953; Roenigk, H. H. Jr., et al. Arch. Dermatol. 113(12): 1667-1670, 1977; Frappazz, A., et al. Env. J. Dermatol. 1993, 3: pág. 351-354; Mozzanica, N., et al. Acta Dermatol. Venereol. 1994, 186: pág. 171-172; Ortonne, J. P.New Dermaytol. 1994, 13: pág. 746-751; Panizonni R. Schweizerische Rundschav fur Medizin Praxis 1995, 84: pág. 649-653; Kirsner, R. S. Am. Fam. Phys. 1995, 52: pages 237-240).

It is known of the state of the art the use of diverse preparations like pitches in petrolatum or alcoholic solutions for the treatment of the psoriasis.

From last century the antialine is used and it has occupied an important roll in the treatment of the illness, but it has the inconvenience of causing irritations of the skin.

In 1925 the ultraviolet radiation was introduced that has continued being used, alone or combined with other medications, but it has its adverse collateral effects.

The psoralens are also used from in the past in spite of their proven toxic effect.

The corticosteroids used in topical way in general have been useful in selected cases, but the tendency to rebound limits their use.

Recently it has been begun to use, but with scarce successes, the retinoids, some anti-metabolites like metotrexate, thioguamne and others.

From the century III it is reported from China the use of the placenta as biological stimulant.

Starting from 1945 the Soviet researcher Filatov developed and consolidated a method to isolate substances with healing properties starting from the animal tissues and vegetables conserved in cold to which he denominated histotherapy. Within of it the placenta occupies an important place (Filatov, V. Ed. Medicina Medguis. URSS, 1945).

Orechkin in 1963, based on studies carried out with 300 sick persons of cutaneous affections, reaches the conclusion that under the influence of the histotherapy the cure of 25% of the cases of an improvement more or less apparent can be obtained in the 38,5% of the same. (Orechkin, Material E. of the Scientific Conference dedicated to the 30 anniversary of V. Filatov's histotherapy method. Kiev: 12, 1963).

The mechanism of therapeutic action of the biogenic stimulators of the psoriasis was ignored. Makarov and Romani pointed out that under its effects the formation of suprarenal corticoids it is intensified and using the experimental theory with the paws of the rats demonstrated that they also possesses anti-inflammatory action therefore being able to behave in a same way that these hormones (Makarov and Romani. Comp. Rend. Soc. Biol. 1951, 1966: 4-626).

The therapeutic means for the treatment of this illness have varied according to their localization, graveness, duration, previous treatments and the patient's age.

Of the many resources with which the medicine has to combat the psoriasis, the placental histotherapy is one of the most effective and however one of the less well known.

Disclosure of the invention.

The present invention is related with an extract obtained starting from the human placenta, which is incorporated in a hydrosoluble gel, and that it is constituted in a medication of having proven effectiveness for the treatment of the psoriasis.

Although the route of administration preferably for these stimulators is the parenteral one, in the present invention it is provided the topical application of this hydrosoluble gel that contains the mentioned active principle.

Therefore, the present invention is related with a hydrosoluble gel that contains as active principle a mixture of unsaturated and poly-unsaturated fatty acids obtained from the human placenta, which intervene in the regulation of the speed of regeneration of the epidermis, after to its

transcutaneous absorption from the application place, of here its anti-psoriatic action.

For the obtaining of the active principle useful in the treatment of the psoriasis, the following operations are carried out:

- starting from frozen placentas, previously washed for their separation from the amniotic membrane and the umbilical cord, their cotyledons are separated which are washed again with abundant water;
- the mass of cotyledons is milled to achieve particles of approximately 12 mm of diameter;
- the solid is again washed by means of agitation in water and later on filtered by gauze, being milled again until a particle size between 2 and 6 mm of diameter;
- the obtained mass is agitated during 1-3 hours with 1 to 4 volumes of alcohol per mass of cotyledons, passing later by a gauze;
- the resultant liquid is rotoevaporated and re-dissolved in a mixture of chloroform methanol in the proportion 4:2, staying in maceration during 24 hours more;
- the obtained product is centrifuged to 2000 rpm, the supernatant is rotoevaporated to dryness and finally it is re-dissolved in ethanol in a proportion 1:1.

For the preparation of the formulation of this active principle as a hydrosoluble gel, they are dissolved between 25.5 and 55.8 g of the human placenta extract obtained, in a hydrosoluble excipient constituted by between 35 to 50 g of purified water, between 0.10 to 0.30 g of methyl-paraben and 0.01 to 0.05 of propyl-paraben, to those previous to the addition of the active principle they are added under agitation between 2 to 5 g of carboximetylcellulosa and between 5 to 20 g of glycerin.

To the human placenta extract PE-100 it was determined its composition, finding that it is constituted fundamentally by unsaturated and fatty acids as palmitoleic, and oleic and poly-unsaturated fatty acids as linoleic, arachinoidic and eicosietienoic.

These poly-unsaturated fatty acids are closely related with the therapy of the illness, inhibiting the excessive reproduction of the epidermic cells. Their acceptance for the patients treated evidence the possibility that the composition is broadly used for the proposed application, since so far there is not any report of another product that cures the psoriasis with the innocuousness of the composition of the present invention.

According to clinical reports obtained from the patients, it lacks of noxious secondary effects not only local but also symptomatic.

To determine the effectiveness of the medication, they were carried out open non randomized studies applying as treatment the hydrosoluble gel obtained from the placental extract in the universe of the patient suffering psoriasis.

The Histotherapy Placental Center controlled one of the trials, wherein they were evaluated a total of 400 patients.

To the 2 years of treatment with the medication it was observed a 78% of satisfactory evolution of these patients treaties during this stage.

Another clinical study was carried out with 26 diagnosed patients of psoriasis in a hospital. In the evaluation of the treatment they presented total clearing of the lesions 84,6% of the patients, obtaining satisfactory results in this trial.

In 1990 they began to arrive to Cuba children affected by the nuclear accident happened in Chernobil, old USSR, among them not few of them suffered psoriasis. Of them, 56 patients were studied, patients that were refractory to other medications and, as it is described in the literature, the family cases are in general difficult to try. These patients were treated during 3 months and at the end of the treatment the clinical improvement was achieved in more than 90% of the same ones.

Equally the product of the invention was applied to 100 patients of psoriasis treated in other hospital. Concluded the trial during a period of 6 years, the remission of the illness was achieved in 78% of the cases without registering secondary or symptomatic reactions, neither to take place relapse in 50% of these.

EXAMPLES:

Example 1: Description of the process of elaboration of the extract PE-100.

The defrosted placentas are cleaned by removing the umbilical cord and the amniotic membrane, remaining only the cotyledons, which are washed with abundant water. The mass of cotyledons is milled in the mill until achieving particles between 8 and 12 mm of diameter.

The solid moves to the area of reactors by means of rolling tank and the reactor of 1600 L is loaded adding to it between 2-4 volumes of raw water; it is agitated between 2 to 8 minutes and filtered using gauze and milled later up to achieve particles of size between 2 and 6 mm of diameter. Afterwards, the solid is weighted and the 1600 L reactor is loaded with alcohol (1 to 4 volumes of alcohol per Kg of mass of cotyledons. The mixture is agitated from 1 to 3 hours and then it is passed through gauze. The resultant liquid is rotoevaporated and it is re-dissolved in a mixture of chloroform-methanol in a rate of 4:2, keeping it in maceration during 24 hours. Afterwards it is centrifuged to 2000 rpm and the supernatant is rotoevaporated up to dryness and re-dissolved in ethanol in proportion 1:1, being obtained by this way the active principle that is denominated Placental Extract-100 (PE-100).

When the PE-100 is approved by the laboratories of chemical, biological and microbiological controls, it is proceeded to the production of the hydrosoluble gel.

Example 2: Preparation of a hydrosoluble gel that contains a human placenta extract.

The reactor Olsa is loaded by means of one Bar of vacuum, with the purified water dedicated to the production.

The methyl and propy-lparaben are warmed until their dissolution by means of agitation. The carboximethylcellulosa is mixed with the glycerin during 1 to 3 hours before the beginning of the process to achieve a correct levigate. When the solution is cooled to 30-60°C, the carboxymethylcellulose is incorporated with the glycerin, maintaining constant agitation, incorporating

the PE-100 later with soft agitation until having a gel of uniform aspect, taking samples for the control of the process. Once checked for the technological area some samples are taken to carry out the chemical, biological and microbiological controls and by this way to determine the quality of the production batch.

Example 3: Use of a gel of human placenta extract used through topical way in the treatment of the psoriasis.

The hydrosoluble gel obtained in the Example 2 is used as topical medication in 100 patients of psoriasis belonging to the Service of Dermatology of the General Hospital "Calixto García", in Havana City.

This gel is applied topically with the fingers on the psoriatic lesions, without rubbing, extending it in form of a fine layer.

Its application is carried out with an interval of time of 8 hours, and one of these applications should be accompanied by a previous and later exposition to infrared light during 30 minutes.

Concluded the trial at the end of 2 years, the remission of the illness was achieved in 78% of the cases, without registering local or systemic secondary reactions, neither to take place relapses in 50% of these.

An example of the results achieved in sick persons treated with the composition of the present invention is shown in the Figure 1.

Example 4: Irritation studies in skin.

The test consisted in the daily dermal application of the anti-psoriatic gel during 90 days, to rats Sprague Dawley (SPF), with the objective to evaluate the risks and/or benefits of the treatment with this substance.

Finished the test, in consideration of the pathology results obtained, in particular those of comparative evaluation of the corporal weight and the weight of the organs and their relationship with the absolute weight, as well as the morphological changes (macro and microscopic), it is concluded that the lesions don't respond to direct effects caused by the substance tested in the formulation used and that the repeated application of the same on the shaved skin was innocuous.

Example 5: Study of the histological modifications observed in psoriatic plates tried with the hydrosoluble gel of human placenta extract.

They were carried out biopsies in diverse regions of the body affected by psoriatic lesions in the sick persons, before and three months after the daily topical treatment with the gel of human placenta extract, with the purpose of observing the histological modifications produced.

As remission indexes the values were considered the values in micrometer of the high of the interpapilar epidermic crests and the thickness of the horny layer of the total size of the epidermis sample.

The fragments of tissues were processed, not only for the classic technique of double coloration with hematoxilin-eosin, but also for azan.

The numeric data underwent the t-Student statistical analysis of the average comparison by means of a computer program.

The obtained results demonstrated a significant reduction of the corresponding average values, not only of the horny layer but also of the crests, in eight of the studied cases, that which confirms the effectiveness of the treatment statistically.

Only two patients didn't show some improvement, observing a correspondence between the histological finding and the evaluation of their clinical square.

Example 6: Pharmacological evaluation of diverse anti-psoriatic drugs by means of an experimental model.

The anti-psoriatic activity of the substances to evaluate was carried out according to the experimental model of Spaerman and Jarret (Pharmacological assay for anti-psoriatic drugs. Br. J. Dermatology 92: 581.1975) that bears the topical application of the same on the mouse line.

These substances should diminish the epidermis of the anatomical structure significantly in these animals, if they possess such an effect.

For the trail they were used 35 albino males mice of 20-25g of weight, separated in seven groups of five animals each one, those that were denominated A, B, C, D, E, F and G.

The group A was not treated with any substance to be used as control and to allow the comparison with each one of the substances to study.

The remaining groups were treated in the following ways:

Group B: Desonide ointment.

Group C: Tegrin ointment.

Group D: Gel of human placental extract.

Group E: Betametasone ointment.

Group F: Vitamine A in oil.

Group G: Ointment of pitch.

All the substances were applied topically with the fingers of the operator covered with a rubber thimble, on the tails of the mice starting from one cm of their proximal extreme, covering an extension of 2,5 cm of their longitude in their entire contour.

The time of duration of the topical treatment was of 21 days for all the groups, except the control that didn't receive any treatment.

Lapsed this time the animals were sacrificed to extract them the skin segment that covers the tail in an extension of 3 cm and to carry out the corresponding histological study, for which the skin is lengthwise cut along its surface and it is extended immediately.

The tissue samples are fixed in ethanol to 70% and are included in blocks of paraffin to cut them sagittally in sections of 7 microns of thickness and later on to stain them by means of the habitual technique of Hematoxiline-Eosine.

The epidermis thickness the sample is measured with an ocular micrometer. They were carried out 10 measurements in 10 different regions randomly selected by each line, so that 50 measurements were obtained by each treatment type and for the control

According to the results obtained by means of this study it could be proven that the four substances habitually used in the treatment of the psoriasis (B,

C, E and G) significantly diminish the epidermis thickness in the tail of the mouse, regarding the control group, non subjected to any treatment.

It is proven that, on the contrary, the vitamin A eventually used possibly in the treatment of the psoriasis can have a noxious effect in this sense when increasing the epidermis thickness in a statistically significant way.

Jointly it could also be evidenced that the gel of placental extract, object of the invention, reduces significantly as the previous substances the epidermis thickness of the mouse line, what facilitates the inclusion of this formulation inside the therapeutic arsenal for the treatment of this illness.

The results obtained in this study are shown in the Figure 2.

Example 7: Evaluation of a gel of human placenta with anti-psoriatic action.

A hydrosoluble gel is used with base on Carboxymethylcellulose, Propylene glycol and distilled water which is added an alcoholic extract of human placenta, with the purpose of evaluating the anti-psoriatic action thereof, using it as topical medication in 26 patients carrier of psoriasis. Concluded the trial at the end of 2 years, the remission of the cutaneous lesions was achieved in 22 patients (84,6%), marked improvement in 3 patients for 11,5% and a patient (3,8%) it didn't present change in its lesions.

On the other hand, it was observed that adverse reactions were not presented to the use of the medication.

Example 8: Clinical and histological studies of a group of children of Chernobyl tried with the anti-psoriatic gel.

The formulation of the invention is used with the purpose of evaluating the anti-psoriatic action of this gel, using it as topical medication in 56 patients of psoriasis affected by this illness after of the Chernobyl nuclear accident.

The results of the treatment were evaluated in the patients of psoriasis during 3 months. When concluding the treatment the anti-psoriatic gel had demonstrated its effectiveness, achieving the clinical and histological improvement in more than 90% of the patients, without being reported in any case undesirable collateral effects.

Example 9: Evaluation of the use of the formulation of the invention in the Histotherapy Placental Center' s Clinic.

A hydrosoluble gel is used with base on Carboxymethylcellulose, Propylene glycol and distilled water which is added an alcoholic extract of human placenta with bio-stimulant properties with the purpose of evaluating the anti-psoriatic action of the same, using it as topical medication in 400 patients carrying psoriasis that went to the Service of Dermatology of the Clinic belonging to the Histotherapy Placental Center.

The general objective was to know the therapeutic effectiveness of this gel elaborated starting from human placenta in its topical use, in patients with psoriasis. It specific objective was to determine the clinical evolution of the patients treaties and to specify presence or not, of possible adverse reactions to the use of the product.

Concluded the study at the end of 2 years, the remission of the cutaneous lesions was achieved in the patients 78% and it was observed that adverse reactions were not presented to the use of the medication.

Brief Description of the Figures:

Figures 1: It represents the evolution of a patient with psoriatic lesions widespread, before (A) and three months after the topical treatment with the gel of placental extract (B).

Figures 2: The figure 2 shows the results obtained in the determination of the anti-psoriatic activity of substances to evaluate, according to the experimental pattern of Spaerman and Jarret.

The substances were evaluated in seven animal groups denominated A, B, C, D, E, F and G in correspondence to the treatment to that they were subjected.

The group A it was not treated with any substance (placebo) and the remaining groups were been in the following ways:

Group B: Desonide ointment.

Group C: Tegrin ointment.

Group D: Gel of placental extract human.

Group E: Betametasone ointment.

Group F: Vitamin A in oil.

Group G: Ointment of pitch.

SERVICIOS JURIDICOS
LEX S.A.
MARCAS Y PATENTES

CLAIMS

1. Composition for topical application for the treatment of the psoriasis containing an alcoholic extract derived from human placenta as active principle, and an appropriate excipient.

2. Composition according to claim 1 wherein this derived alcoholic extract of the human placenta is constituted fundamentally by unsaturated fatty acids such as palmitoleic and oleic acids and poly-unsaturated fatty acids such as linoleic, arachinoidic and eicosietienoic acids.

3. Composition according to claims 1 and 2 wherein for each 100 grams of composition it contains approximately 59 ml of this alcoholic extract in an hydrosoluble excipient.

4. Composition according to claims 1 to 3 wherein it is a hydrosoluble gel.

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AMAR, PLAYA.
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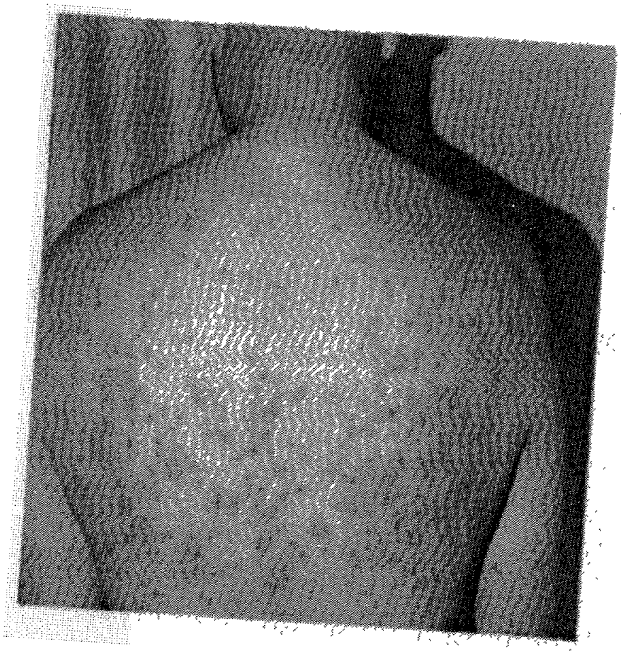
ail: lexsa@colombus.cu

FIGURE 1.

(A)



(B)

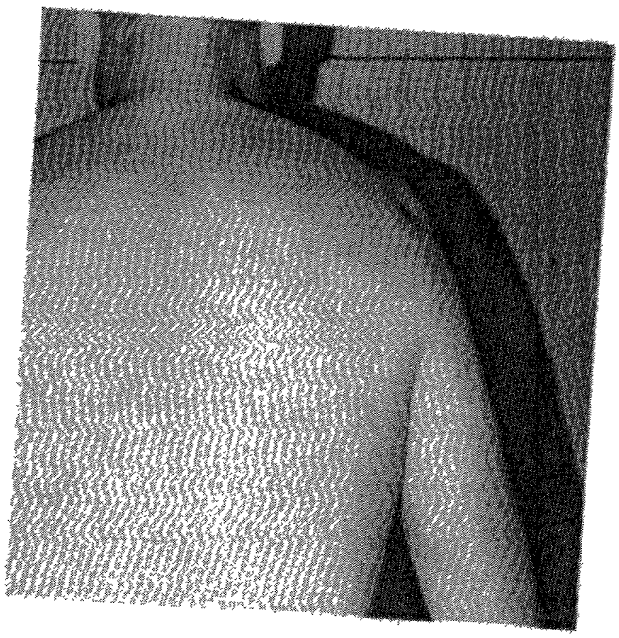
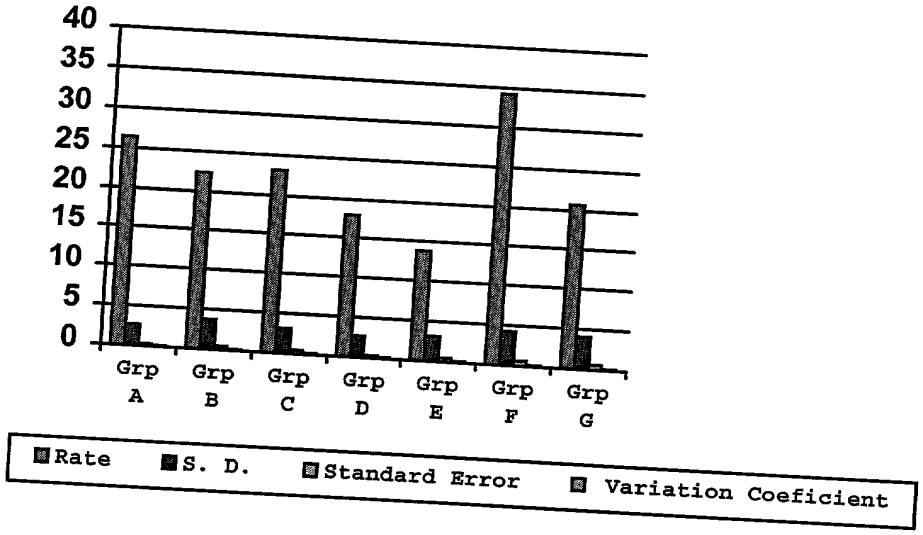


FIGURE 2.



Applicant or Patentee: Carlos Manuel Miyares Cao
Serial or Patent No.: 09/914,257
Filed or Issued: 8/22/2001
For: Composition for the Treatment of Psoriasis

P-24LEXSA
Docket No.: #3

DECLARATION CLAIMING SMALL ENTITY STATUS

[37 CFR 1.9(f) and 1.27(C)]

SMALL BUSINESS CONCERN

I hereby declare that I am

- [x] the owner of the small business concern identified below:
- [ ] an official of the small business concern empowered to act on behalf of the concern identified below

NAME OF CONCERN:

ADDRESS OF CONCERN:

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled: Composition for the Treatment of Psoriasis

described in

- [ ] the specification filed herewith
- [x] application serial no. 09/914,257, filed 8/22/2001
- [ ] patent no. , issued

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

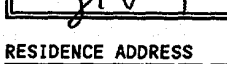
Note: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

FULL NAME: Carlos M. Miyares Cao ADDRESS: Autopista Novia del Mediodía y 173, La Lisa, Havana, Cuba	[ ] INDIVIDUAL [x] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION
FULL NAME: ADDRESS:	[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION
FULL NAME: ADDRESS:	[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified declaration is directed.

NAME OF PERSON SIGNING	TITLE
Carlos M. Miyares Cao	Director

SIGNATURE	DATE
	September 14, 2001

RESIDENCE ADDRESS

Ave. 3ra No. 03 entre 0 y 2, Miramar, Playa, C. Habana, Cuba.

#3

UNITED STATES -- PATENT
DECLARATION FOR PATENT APPLICATION

Attorney's Docket No.: P-24LEXSA

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

the specification of which

(check one) ☐ is attached hereto. I.A. Filing Date 2/22/2000

☒ was filed on 8/22/2001 as 09/914,257

Application Serial No.: 09/914,257,

and was amended on _____ *(if applicable)*.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s):

Appln. No.	Country	Date Filed	Priority Claimed
☐ PCT/CU00/00001	PCT	2/22/2000	☒ YES ☐ NO
☐ CU16/99	Cuba	2/22/1999	☒ YES ☐ NO
☐			☐ YES ☐ NO

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56(a) which became available between the filing date of the prior application and the national or PCT international filing date of this application:

Appln. Serial No.	Filing Date	Status: Patented, Pending, Abandoned
		☐ Patented ☐ Pending ☐ Abandoned
		☐ Patented ☐ Pending ☐ Abandoned
		☐ Patented ☐ Pending ☐ Abandoned

POWER OF ATTORNEY

I hereby appoint the following attorney(s) and/or agent(s) to prosecute the application entitled
Composition for the Treatment of Psoriasis
and to transact all business in the Patent and Trademark Office connected therewith:
HENRY A. MARZULLO, JR., Reg. No. 20,910; MARVIN FELDMAN, Reg. No. 25,797
HOWARD N. ARONSON, Reg. No. 27,302; and
MYRON GREENSPAN, Reg. No. 25,680.

Address all telephone calls to *Myron Greenspan,* at telephone number (914) 723-4300, or to the attorney executing the last document. Address all correspondence to **LACKENBACH SIEGEL MARZULLO ARONSON & GREENSPAN, P.C.** at **Penthouse Suite, One Chase Road, Scarsdale, New York 10583 U.S.A.**

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full Name of First or Sole Inventor Carlos M. Miyares Cao	Citizenship **Cuban**
RESIDENCE Address -- Street Ave. 3ra No. 03 e/ 0 y 2, Miramar, Playa, C. Habana, Cuba.	POST OFFICE Address -- Street **(same as residence)**
City (Zip) Ciudad Habana	City (Zip) Same es residence CUX
State or Country Cuba	State or Country Same as residence
Date September 14, 2001	Signature

Full Name of Second Joint Inventor	Citizenship **Cuban**
RESIDENCE Address -- Street	POST OFFICE Address -- Street **(same as residence)**
City (Zip)	City (Zip)
State or Country	State or Country
Date	Signature

Full Name of Third Joint Inventor	Citizenship **Cuban**
RESIDENCE Address -- Street	POST OFFICE Address -- Street **(same as residence)**
City (Zip)	City (Zip)
State or Country	State or Country
Date	Signature

☒ **Additional inventors are being named on separately numbered sheets attached hereto.**